(S236) VISPA-CEL, AN ALLOGENEIC ANTI-CD19 CAR-T CELL THERAPY WITH A PD-1 KNOCKOUT, IN PATIENTS WITH RELAPSED/REFRACTORY B CELL NON-HODGKIN LYMPHOMA (ANTLER PHASE 1 CLINICAL TRIAL)

Topic: 19. Large B cell lymphomas - Clinical

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Background

Vispacabtagene regedleucel (vispa-cel, formerly CB-010) is an allogeneic anti-CD19 CAR-T cell therapy manufactured from healthy donor T cells. The Cas9 chRDNA genome-editing technology is used for three genome edits: (1) KO of *TRAC* to reduce risk of GvHD, (2) insertion of a CD19-specific CAR (FMC63 scFv, 4-1BB), and (3) KO of PD-1 to prevent premature CAR-T cell exhaustion and potentially enhance antitumor activity.

Aims

ANTLER is a Phase 1 trial (NCT04637763) with 3+3 dose escalation and expansion to evaluate the safety and efficacy of vispa-cel in patients (pts) with r/r B-NHL and determine the RP2D.

Methods

All pts received lymphodepletion of sequential cyclophosphamide (60 mg/kg/day x 2 days) then fludarabine (25 mg/m^2/day x 5 days) followed by a single infusion of vispa-cel. Three vispa-cel doses (40 million [M], 80M, and 120M cells) were evaluated in dose escalation and dose expansion. 80M cells was selected as the RP2D. Subsequently, a 2L LBCL confirmatory cohort prospectively evaluated donor-recipient matching ≥4 HLA alleles. A retrospective analysis was performed and identified LBCL pts treated with vispa-cel manufactured from a young donor (<30 yrs) and ≥2 matched HLA alleles, reported as the optimized cohort.

Results

As of Sep 2025, 84 pts received vispa-cel including 67 2L LBCL pts. The median age was 66 years (20-86). Of the 2L LBCL pts, 40 pts (60%) had an aaIPI score of ≥2. Vispa-cel was generally well tolerated and no GvHD was observed. CRS occurred in 55% of pts (1% Gr ≥3), ICANS occurred in 14% of pts (4% Gr ≥3), infections occurred in 51% of pts (25% Gr ≥3), Gr ≥3 prolonged cytopenias occurred in 28% of pts, and immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome occurred in 2% of pts (all Gr≥3). By day 60, the neutropenia and thrombocytopenia recovery to Gr ≤2 was 95% and 86%, respectively. Five patients died due to AEs following vispa-cel. 1 related (IEC-HS at day 25); 1 possibly related (bladder perforation at day 172); 3 deaths unrelated to vispa-cel per investigator were acute respiratory failure/pneumothorax, ARDS, and HHV6 encephalitis. In the 2L confirmatory cohort (N=22), ORR was 82% and CR rate was 64%. Median PFS and DOR were not reached (NR) with a 12-month PFS of 51%. Donor age (<30 yrs) and ≥2 matched HLA alleles were identified as covariates associated with improved PFS. In the optimized cohort (N=35), ORR was 86% and CR rate was 63%. The median PFS and DOR were NR with a 12-month PFS of 53%. In contrast, the median PFS in pts treated with vispa-cel from older donor (≥30 yrs) T cells and with <2 HLA alleles matched was 2.5 months (Figure 1). Peak expansion occurred days 7-10 with persistence up to 30 days post-infusion. Endogenous T and NK cells recovered rapidly in peripheral blood (~4 weeks) post-infusion, with B cell recovery in all pts by ~300 days. Updated clinical data with translational analyses from the optimized cohort will be presented.

Summary/Conclusion

Vispa-cel is an allogeneic CAR-T cell therapy that results in deep and durable responses on par with approved autologous CAR-T cell therapies in 2L LBCL pts with a generally well-tolerated safety profile supporting outpatient administration. Improved PFS was observed in pts treated with vispa-cel manufactured from young donors (<30 yrs) and ≥2 matched HLA alleles. A randomized controlled pivotal trial in 2L LBCL pts who are ineligible for both autologous CAR-T and transplant is being planned.

Figure 1: Partial HLA matching and young donors lead to durable outcomes with vispa-cel in LBCL patients